

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
3 June 2004 (03.06.2004)

PCT

(10) International Publication Number  
**WO 2004/046118 A2**

(51) International Patent Classification<sup>7</sup>: **C07D 239/00**

(21) International Application Number:  
PCT/US2003/014294

(22) International Filing Date: 6 May 2003 (06.05.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/378,329 6 May 2002 (06.05.2002) US

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(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

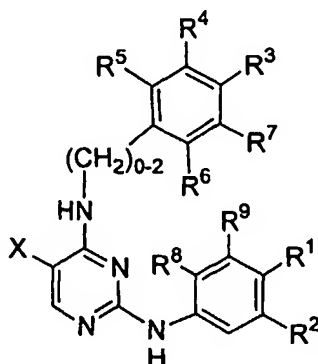
(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

#### Published:

— without international search report and to be republished upon receipt of that report

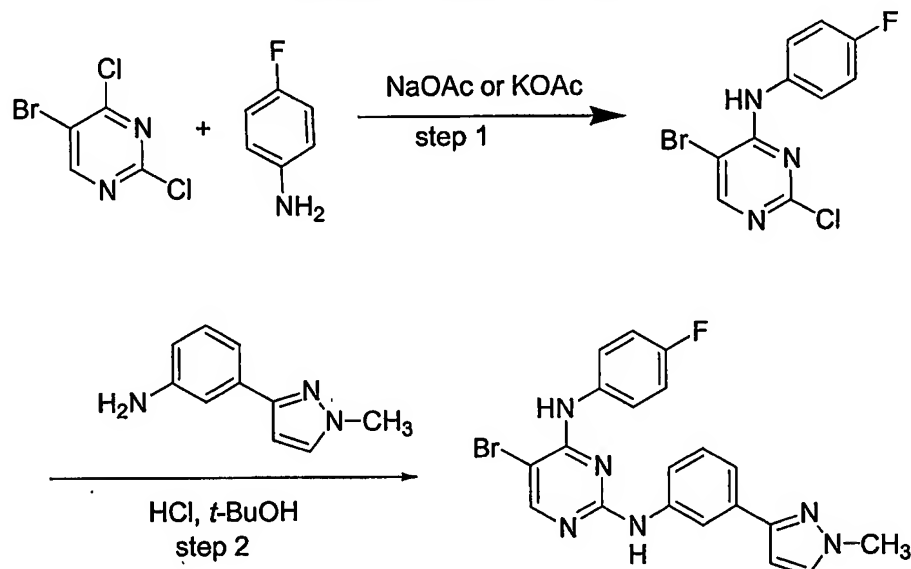
For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: 2-4-(DI-PHENYL-AMINO)-PYRIMIDINE DERIVATIVES USEFUL FOR TREATING HYPER-PROLIFERATIVE DISORDERS



(I)

(57) Abstract: The present invention relates to a 2-4-(diphenyl-amino)-pyrimidinyl compound of Formula I useful for treating hyper-proliferative disorders.

Preparation of Specific Compounds of the InventionExample 1Methods 1a, 1b, 1c, and 1dPreparation of *N*-[5-bromo-4-[(4-fluorophenyl)amino]-2-pyrimidinyl]-*N*-[3-(1-methyl-1*H*-pyrazol-3-yl)phenyl]amineStep 1. Two methods were used:

Method 1a. To a solution of NaOAc (27.0 g, 330 mmol) in water (70 mL) and THF (140 mL), were added 5-bromo-2,4-dichloropyrimidine (25.0 g, 110 mmol) and 4-fluoroaniline (12.2 g, 110 mmol). The mixture was stirred at room temperature for 18 h then saturated NaHCO<sub>3</sub> solution (50 mL) was added and the aqueous layer was extracted with EtOAc (150 mL × 2); the combined organic layers were dried over MgSO<sub>4</sub>; filtered and concentrated under reduced pressure. The residue was treated with 200 mL hexane and filtered to give 5-bromo-2-chloro-4-[(4-fluorophenyl)amino]pyrimidine as a 30.0 g pale yellow powder (90%).

Method 1b. To a solution of K<sub>2</sub>CO<sub>3</sub> (44.5 g, 322 mmol) in water (125 mL) and *i*-PA (375 mL), were added 5-bromo-2,4-dichloropyrimidine (25.0 g, 108 mmol) and 4-fluoroaniline (12.0 g, 107 mmol). The mixture was stirred at room temperature for 18 h then water (3000 mL) was added and the product was precipitated out. Filtered and dried to give 30.0 g (90%) 5-bromo-2-chloro-4-[(4-fluorophenyl)amino]pyrimidine as a pale yellow powder.